REMARKS

The following remarks are submitted as a full and complete response to the Office Action issued on January 26, 2011. Claims 1-16 are currently pending. Reconsideration of all outstanding rejections is respectfully requested in view of the following amendments and remarks.

Amendments

Claim 1 has been amended to recite that the formulation (a) optionally comprises an outer coating and (b) is a 3 or 4 layer tablet. Support for the former amendment can be found in claim 2. Support for the latter amendment can be found throughout the specification, for example, in paragraphs [0015] – [0019] and paragraphs [0030] – [0033] and [0055] of the published application.

Applicants submit that these amendments do not constitute new matter and their entry is requested.

Rejection under 35 U.S.C. §112, first paragraph

The Patent Office has rejected claims 1-16 under 35 U.S.C. §112, first paragraph, for failure to comply with the written description requirement, specifically with respect to the limitations: (a) a sustained release formulation is a three-layer containing tablet and (b) the sustained release core comprises a mixture of an active ingredient and a polymer having erosion and swelling property in mammalian intestinal secretions. Applicants traverse this rejection.

Without acceding to the propriety of this rejection, claim 1 has been amended to replace "three-layer containing tablet" with "3 or 4 layer tablet." Applicants submit that this amendment obviates the written description rejection with respect to this language of the claims.

The Patent Office contends that the application does not provide a written description of the subject matter that a "sustained-release comprises a mixture of an active ingredient and a polymer having erosion and swelling property in mammalian intestinal secretions," because the application describes the use of additional ingredients in the description of making the sustained-release core. Because of the disclosed process, the Patent Office contends that the language of

the claim is a broadening of the claimed subject matter that is not adequately supported either explicitly or implicitly in the original disclosure. Applicants submit that the Patent Office is in error in this rejection.

The specification clearly describes a sustained-release formulation that includes (i.e., comprises) a sustained-release core including (i.e., comprising) "an active ingredient and a polymer having erosion and swelling property in mammalian intestinal secretions." See, paragraphs [0016] and [0031] of the published application. In addition, the specification clearly describes that the sustained-release core "may include common additives, in addition to the active agent and the polymer." See paragraph [0040] of the published application. In view of these passages in the specification, Applicants submit that it is clear to the skilled artisan that they were in possession of (a) a sustained-release core that comprises an active agent and a polymer with erosion and swellable properties in mammalian intestinal secretions and (b) a sustained-release core that comprises an active agent, a polymer with erosion and swellable properties in mammalian intestinal secretions and common additives, such as a diluent, a disintegrating agent, a binder, solvent, lubricant. Thus, the specification provides a written description of a sustained-release core comprising the active agent and the specified polymer.

Furthermore, Applicants submit that it is clear to the skilled artisan that they were in possession of (a) a sustained-release core comprising a **mixture** of the active ingredient and a polymer with erosion and swellable properties in mammalian intestinal secretions and (b) a sustained release core comprising a **mixture** of the active ingredient, a polymer with erosion and swellable properties in mammalian intestinal secretions and common additives, such as a diluent, a disintegrating agent, a binder, solvent, lubricant. Applicants submit that it is clear to the skilled artisan reading the specification that these ingredients must be in a mixture in order for the sustained-release core to comprise the specified ingredients. The fact that the ingredients in the sustained-release core, as well as the ingredients in each of the coatings, are in a mixture is illustrated in the Examples. In addition, the Patent Office concludes at pages 7 and 10 of the Office Action that Shinoda (cited in the rejection under Section 103) discloses a mixture of a drug and a polymer on a coated particle. Such a disclosure of a mixture must come from the disclosures in Shinoda of "adding a polymer solution to drug and microcrystalline cellulose"

(paragraph [0054]) or "drug is layered and coated on commercial crystalline cellulose particles … using a binder, such as hydroxypropylmethyl cellulose" (paragraph [0074]) or drug and hydroxypropylmethyl cellulose dissolved in water and methanol (paragraph [0116]). If these passages in Shinoda disclose a mixture of the substances to the skilled artisan, then Applicants submit that a "sustained-release core including an active ingredient and a polymer … " (paragraph [0031] of Applicants' published application) also establishes to the skilled artisan that Applicants were in possession of such a mixture as set forth in part (a) of claim 1.

Thus, Applicants submit that the originally filed specification and claims clearly shows to the skilled artisan that they were in possession of a sustained-release core that comprises a mixture of an active ingredient and a polymer having erosion and swelling property in mammalian intestinal secretions. That is, Applicants submit that the specification as originally filed describes the invention in such a way as to reasonably convey to one skilled in the relevant art that Applicants had possession of the claimed invention.

In view of the above amendments and remarks, Applicants submit that the claimed subject matter is fully described in the written description of the present application, and thus satisfies the requirements of 35 U.S.C. §112, first paragraph. Withdrawal of this rejection is requested.

Rejection under 35 U.S.C. §103(a)

The Patent Office has rejected claims 1-16 under 35 U.S.C. §103(a) as being unpatentable over Shinoda et al. (U.S. Publ. Appln. No. 2003/0147948) ("Shinoda"). The Patent Office contends that Shinoda teaches that sustained-release particles are formulated by layering the drug onto a core particle (i.e., commercial crystalline cellulose particles, crystalline lactose, granular sugar, sodium chloride, silicone dioxide, etc.) using a binder such as hydroxypropyl methylcellulose, wherein the particle is then further coated with a polymer substance such as an enterosoluble polymer substance, and then a polymer substance with drug may be layered onto the particles. The Patent Office contends that the claimed subject matter is obvious from the teachings of Shinoda. Applicants respectfully disagree.

As currently amended, claim 1 recites a sustained-release formulation that "is a 3 or 4 layer tablet", in which a sustained-release core comprises a mixture of an active ingredient and a polymer having erosion and swelling property in mammalian intestinal secretions. The 3 or 4 layer tablet is (1) a sustained-release core, (2) an enteric film coating layer coated on the sustained-release core, (3) an active ingredient-containing film coating layer coated on the enteric film coating layer and comprising the active ingredient and a hydrophilic polymer for film coating and optionally (4) an outer coating layer coated on the active ingredient-containing film coating layer and comprising a film coating polymer selected from the group consisting of a hydrophilic polymer, a hydrophobic polymer, a pH-dependent polymer, and a combination thereof. Thus, when items (1)-(3) are present, the claimed formulation is a 3 layer tablet, and when items (1)-(4) are present, the claimed formulation is a 4 layer tablet. Applicants submit that this sustained-release formulation is not taught or suggested by Shinoda.

Specifically, the sustained-release particles of Shinoda are formulated by "layering the drug onto a core particle using a binder such as hydroxypropyl methylcellulose." These sustained-release particles of Shinoda are different from the claimed sustained-release core comprising a mixture of an active ingredient and a polymer having erosion and swelling property in mammalian intestinal secretions, because the drug layered on the core in Shinoda produces a particle with 2 layers, i.e., a particle core and a drug containing layer. Because Shinoda does not describe a core comprising a mixture of an active agent and the specified polymer as a single layer as in the claimed invention, Shinoda does not describe or suggest this element of the claimed sustained-release formulation.

Shinoda then coats the resulting particle with a polymer, which the Patent Office notes may be an enterosoluble polymer. The addition of this layer to the previously coated particle produces a formulation with 3 layers, i.e., a particle, a coating comprising a drug and a polymer and a coating comprising an enterosoluble polymer. Because this 3 layer formulation of Shinoda does not include a coating comprising an active agent and a polymer, this element of the claimed invention is missing from the 3 layer formulation of Shinoda. In addition, the 3 layer formulation of Shinoda is not a 3 layer tablet as set forth in the claimed invention, rather it is a

particle with two layers. Thus, this element of the claimed invention is also missing from Shinoda.

The Patent Office asserts that Shinoda then adds a further coating which comprises an active agent and a polymer, which the Patent Office notes may include a hydrophilic polymer. Assuming that this interpretation of Shinoda is proper, Applicants submit that the particle with this additional coating produces a formulation that has 4 layers. This 4 layer formulation is different from the claimed 4 layer tablet because the claimed 4th layer is an outer coating layer which comprises a polymer. This layer is not described by Shinoda. Thus, this element of the claimed invention is missing from Shinoda. In addition, the 4 layer formulation of Shinoda is not a 4 layer tablet as set forth in the claimed invention, rather it is a particle with three layers. Thus, this element of the claimed invention is also missing from Shinoda.

Furthermore, Applicants submit that the Patent Office's interpretation of Shinoda is not correct. Paragraph [0074] of Shinoda describes the process for making the sustained-release fine particles used to make the tablets. Three options for coating particles are provided by Shinoda in this paragraph. First,

> drug is layered and coated on commercial crystalline cellulose particles, crystalline lactose, granular sugar, sodium chloride, silicon dioxide, and the like, using a binder such as hydroxypropylmethyl cellulose, and the like …

Second,

> It is also possible to layer and coat a polymer substance, such as water-insoluble polymer substance, gastrosoluble polymer substance, enterosoluble polymer substance, wax-like substance, and the like, together with drug on commercial crystalline cellulose particles, crystalline lactose, granular sugar, sodium chloride, silicon dioxide, and the like to make sustained-release fine particles.

Third,

> Sustained-release fine particles are also made by the agitation granulation method or tumbling fluidized granulation method after adding a solution of polymer substance to drug and microcrystalline cellulose.

According to the process described in this paragraph, the particles that have been coated by either one of these methods are then further coated. In describing this further coating in context of the first option, paragraph [0074] of Shinoda states

> and then a polymer substance, such as water-insoluble polymer substance, gastrosoluble polymer substance, enterosoluble polymer substance, wax-like substance, and the like, is further coated on this to make sustained-release fine particles.

After describing the second and third options for coating the particles, paragraph [0074] of Shinoda states

> The above-mentioned coating can be further performed on these sustained-release fine particles, and they can be given enterosoluble function by coating with enterosoluble polymer base as necessary.

This nature of the particles of Shinoda is further confirmed by the Examples. For instance, Examples 1, 7 and 9 describe the preparation of sustained-release particles in which the drug is tamsulosin hydrochloride and which contain three layers coated on the starting particles. According to these Examples, the sustained-release particles comprise particles with a drug/polymer coating (specifically hydroxypropylmethyl cellulose), further coated with a polymeric coating (specifically, ethyl cellulose and hydroxypropylmethyl cellulose) and then coated with an enteric coating (specifically Aquacoat, Eudragit L30D55 and Eudragit NE30D). Applicants submit that it is exceedingly clear to the skilled artisan that Shinoda does not describe a particle which contains a drug/polymer layer, an enterosoluble polymer layer and a further drug/polymer layer. Instead, the particles of Shinoda contain only a single drug/polymer layer with up to two additional coating layers, neither of which contains the drug. Thus, Shinoda is lacking element (c) of the claimed subject matter.

Examples 3-6 and 8 describe sustained-release particles in which the drugs are acetaminophen and nicardipine hydrochloride, respectively. The sustained-release particles of these Examples comprise particles with a drug/polymer coating (specifically hydroxypropylmethyl cellulose) further coated with a polymeric coating (specifically, ethyl cellulose and hydroxypropylmethyl cellulose). These sustained-release particles also contain only a single drug/polymer layer with one additional coating layer, which does not contain the drug. These Examples also demonstrate that Shinoda is lacking element (c) of the claimed subject matter.

According to Shinoda, the particles are then granulated with filler and binder (see paragraph [0076]) and finally formed into tablets (see paragraph [0080]). Thus, the tablets of

Shinoda are not a 3 or 4 layer tablet, but instead are tablets containing sustained-release particles, binder and filler. The tablets containing these elements, in essence, form a single sustained release core which is the only layer of the tablets described by Shinoda. There are no layers within the tablets of Shinoda. Applicants submit that the skilled artisan reading Shinoda clearly understands that Shinoda describes coated particles that are used for preparing tablets. The skilled artisan knows that coated particles are not tablets, but are used for form tablets. The claimed subject matter is directed to a 3 or 4 layer tablet and not a single tablet containing particles that have 3 or 4 layers, one of which is the particle core. Accordingly, Shinoda fails to teach or suggest the elements of the claimed subject matter. Thus, it is clear that Shinoda does not disclose or suggest the claimed subject matter.

In comparison with the formulation of Shinoda, the formulation recited in claim 1 of the present application is a 3 or 4 layer tablet comprising a sustained release core, an enteric film coating layer, and an active ingredient-containing film coating layer (3 layer tablet) and optionally an outer coating layer (4 layer tablet). Shinoda does not disclose or suggest any such sustained-release 3 or 4 layer tablet having the layers specified in claim 1. Furthermore, Shinoda discloses tableting the layered particles which does not produce a 3 or 4 layer tablet. Accordingly, Shinoda fails to teach or suggest the elements of the claimed subject matter.

The following comparison shows the differences between the sustained-release formulation of Shinoda and the claimed subject matter.

Layer	Shinoda	Claimed Subject Matter
1	particle, e.g., crystalline cellulose	sustained-release core comprising mixture of drug and a polymer having erosion and swelling property in mammalian intestinal secretions
2	drug coated on particle using a polymer, such as hydroxypropylmethyl cellusose (a polymer having erosion and swelling property in mammalian intestinal secretions)	an enteric film coating layer coated on the sustained-release core
3	polymer coating, such as water-insoluble polymer substance gastrosoluble polymer substance,	an active ingredient-containing film coating layer coated on the enteric film coating layer and comprising the active ingredient

	enterosoluble polymer substance, etc.	and a hydrophilic polymer for film coating
4	enterosoluble polymer coating as necessary	an outer coating layer coated on the active ingredient-containing film coating layer and comprising a film coating polymer selected from the group consisting of a hydrophilic polymer, a hydrophobic polymer, a pH-dependent polymer, and a combination thereof

As seen in this comparison, the formulations of Shinoda and the present invention are entirely different with respect to each element. Although Applicants submit that a particle with a drug coating is not the same as or equivalent to a sustained-release core comprising the drug and specified polymer, a comparison of such a non-equivalent formulation also shows that the formulations are different.

Layer	Shinoda	Claimed Subject Matter
1	particle, e.g., crystalline cellulose with drug coated on particle using a polymer, such as hydroxypropylmethyl cellusose (a polymer having erosion and swelling property in mammalian intestinal secretions)	sustained-release core comprising mixture of drug and a polymer having erosion and swelling property in mammalian intestinal secretions
2	polymer coating, such as water-insoluble polymer substance gastrosoluble polymer substance, enterosoluble polymer substance, etc.	an enteric film coating layer coated on the sustained-release core
3	enterosoluble polymer coating as necessary	an active ingredient-containing film coating layer coated on the enteric film coating layer and comprising the active ingredient and a hydrophilic polymer for film coating
4		an outer coating layer coated on the active ingredient-containing film coating layer and comprising a film coating polymer selected from the group consisting of a hydrophilic polymer, a hydrophobic polymer, a pH-dependent polymer, and a combination thereof

As seen in this comparison, layer 3 of Shinoda is not the same as layer 3 of the claimed subject matter.

As discussed above, the resulting sustained-release particles of Shinoda are not tablets, but are combined with a binder and a filler to make tablets. The tablets of Shinoda do not have the 3 or 4 layers required by the claims. Accordingly, Shinoda does not disclose or suggest a sustained-release formulation that is a 3 or 4 layer tablet. Thus, Applicants submit that the formulation recited in claims 1-16 of the present application is not rendered obvious by Shinoda.

In view of the above amendments and remarks, Applicants submit that Shinoda does not render the claimed subject matter obvious. Accordingly, Applicants request withdrawal of this rejection.

Conclusion

In view of the above amendments and remarks, Applicants submit that the claimed subject meets all of the requirements of the patent statutes and is patentable over the prior art. Applicants further submit that the instant application is in condition for allowance. Thus, Applicants respectfully request reconsideration and early allowance of the instant application.

The Commissioner is hereby authorized to charge any fees or credit any overpayment to Deposit Account No. 02-2135.

Respectfully submitted,

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